

PCT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 18 December 2000 (18.12.00)	Applicant's or agent's file reference 365.300
International application No. PCT/US00/05928	Priority date (day/month/year) 30 April 1999 (30.04.99)
International filing date (day/month/year) 08 March 2000 (08.03.00)	
Applicant PIZZA, Mariagrazia et al	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

22 November 2000 (22.11.00)

in a notice effecting later election filed with the International Bureau on:

2. The election was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Nestor Santesso Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 365.300	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/ 05928	International filing date (day/month/year) 08/03/2000	(Earliest) Priority Date (day/month/year) 30/04/1999
Applicant CHIRON CORPORATION et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

contained in the international application in written form

filed together with the international application in computer readable form.

furnished subsequently to this Authority in written form.

furnished subsequently to this Authority in computer readable form.

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2 Certain claims were found unsearchable (See Box I)

3 Unity of invention is lacking (see Box II).

4 With regard to the **title**,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5 With regard to the **abstract**,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6 The figure of the **drawings** to be published with the abstract is Figure No.

as suggested by the applicant.

because the applicant failed to suggest a figure.

because this figure better characterizes the invention.

1

None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/05928

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

- 1 Claims Nos.: 16, 17 (partly)
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(v) PCT – Presentation of information (insofar as related to computer databases)

- 2 Claims Nos.: 5, 6, 15 (completely), 1-4, 7-14, 16-24 (partly)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

- 3 Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

- 1 As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

- 2 As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

- 3 As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 5,6,15 (completely), 1-4, 7-14, 16-24 (partly)

- 1) Claims 5 and 6 (and thus 15 which refers to claim 6 and whose reference to claims 7 and 8 is wrong) lack any essential technical feature which could allow a meaningful search to be carried out. They have thus not been searched. For the same reason claims 18-24 have not been searched insofar as referring to any of claims 5, 6 and 15.
- 2) Claims 1-4, 7-14, 16-24 have only been searched insofar as related to the full sequence SEQ ID 1 in view of the absence of any indication in the claims as to searchable SEQ IDs corresponding to the "NMB open reading frames". SEQ ID 1 as such is not searchable by means of similarity algorithms since it is too long: the search with respect thereto has thus been carried out based on keywords.
- 3) A further reason for not searching claims 1-4 insofar as related to "NMB open reading frames" is that claim 1 is unclear (Art. 6 PCT). It relates to a method for searching open reading frames "within one or more...NMB open reading frames", which is however technically meaningless.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/05928

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C12Q1/68 C12N15/11 C07K14/22

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 17805 A (RAYMOND NIGEL ;QUINN FREDERICK D (US); US HEALTH (US); RIBOT EFRAI) 30 April 1998 (1998-04-30) the whole document ---	1-4, 7-14, 18-24
X	EP 0 467 714 A (MERCK & CO INC) 22 January 1992 (1992-01-22) claims; example 3 --- -/-	1-4, 7-14, 18-24

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

10 October 2000

Date of mailing of the international search report

19.10.

Name and mailing address of the ISA

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Authorized officer

Luzzatto, E

INTERNATIONAL SEARCH REPORT

International Application No

/US 00/05928

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FLEISCHMANN R D ET AL: "WHOLE-GENOME RANDOM SEQUENCING AND ASSEMBLY OF HAEMOPHILUS INFLUENZAE RD" SCIENCE, US, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, vol. 269, no. 5223, 28 July 1995 (1995-07-28), pages 496-498, 507-51, XP000517090 ISSN: 0036-8075 the whole document ---	1-4, 7-14, 16-24
T	TETTELIN H ET AL: "Complete genome sequence of <i>Neisseria meningitidis</i> serogroup B strain MC58 'see comments!.' SCIENCE, (2000 MAR 10) 287 (5459) 1809-15., XP000914963 page 963 ---	
T	PIZZA M ET AL: "Identification of vaccine candidates against serogroup B meningococcus by whole- genome sequencing 'see comments!.' SCIENCE, (2000 MAR 10) 287 (5459) 1816-20., XP000914964 the whole document ---	
T	PARKHILL J ET AL: "Complete DNA sequence of a serogroup A strain of <i>Neisseria meningitidis</i> Z2491 'see comments!.' NATURE, (2000 MAR 30) 404 (6777) 502-6., XP000918875 the whole document -----	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/05928

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9817805	A 30-04-1998	AU 5426098	A	15-05-1998
EP 0467714	A 22-01-1992	AU 8114091	A 23-01-1992	
		CA 2047043	A 20-01-1992	
		FI 913473	A 20-01-1992	
		JP 6056690	A 01-03-1994	
		MX 9100272	A 28-02-1992	
		NO 912822	A 20-01-1992	
		PT 98381	A 29-05-1992	
		ZA 9105629	A 25-03-1992	
		AU 8113691	A 23-01-1992	
		CA 2050635	A 20-01-1992	
		FI 913475	A 20-01-1992	
		JP 6016569	A 25-01-1994	
		JP 6055679	B 27-07-1994	
		NO 912823	A 20-01-1992	
		NZ 238974	A 23-12-1992	
		PT 98382	A 29-05-1992	
		ZA 9105627	A 25-03-1992	
		AU 8113791	A 23-01-1992	
		CA 2047030	A 20-01-1992	
		FI 913474	A 20-01-1992	
		JP 6041197	A 15-02-1994	
		MX 9100274	A 28-02-1992	
		NO 912824	A 20-01-1992	
		PT 98383	A 30-06-1992	
		ZA 9105628	A 25-03-1992	

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70) 14

Applicant's or agent's file reference 365.300	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/05928	International filing date (day/month/year) 08/03/2000	Priority date (day/month/year) 30/04/1999
International Patent Classification (IPC) or national classification and IPC C12Q1/68		
Applicant CHIRON CORPORATION et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I Basis of the report
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

Date of submission of the demand 22/11/2000	Date of completion of this report 09.07.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Luzzatto, E Telephone No. +49 89 2399 8169



INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

International application No. PCT/US00/05928

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-69,71-122 as originally filed

70 as received on 26/06/2000 with letter of 22/06/2000

Claims, No.:

1-24 as originally filed

Drawings, sheets:

1-18 as originally filed

Sequence listing part of the description, pages:

1-750, filed with the letter of 22.6.00

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/05928

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application.
- claims Nos. 5,6,15,24.

because:

- the said international application, or the said claims Nos. 24 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. 5,6,15.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- the written form has not been furnished or does not comply with the standard.
- the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/05928

citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 7,8
No: Claims 1-4,9-14,16-24

Inventive step (IS) Yes: Claims none
No: Claims 7,8

Industrial applicability (IA) Yes: Claims 1-23
No: Claims

**2. Citations and explanations
see separate sheet**

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/05928

Re Item I

Basis of the opinion

- 1) Sequence listing pages 1-750 filed with the letter of 22/6/00 do not form part of the application (Rule 13^{ter}.1(f) PCT).
- 2) Appendix A has been filed along with the application, however is not part of the description (Art. 3(2) PCT); it should therefore be changed into a figure or be deleted along with any reference thereto.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

- 1) Claims 5, 6 and 15 have not been searched and thus no opinion will be given with respect to whether their subject-matter meets the requirements of Art. 33 PCT. The same applies for claims 18-24 insofar as related to any of claims 5, 6, and 15.
- 2) Claims 1-4, 7-14, 18-24 have only been searched insofar as relating to SEQ ID 1 and will therefore be examined on the basis this limitation.
- 3) Claim 24 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).
- 4) Claims 16 and 17 have not been searched insofar as related to computer databases and will thus not be examined with respect to this feature.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/05928

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1) D1 (EP-A-467714) and D2 (WO-A-9817805) disclose the purification of the entire genomic DNA of *N. Meningitidis* (see D1, ex. 3 and claims, D2, ex. 2, p. 54, l. 2-16, claims). They do not however disclose a sequence as that of SEQ ID 1, to which claims 7 and 8 relate. The subject-matter of the said claims is thus novel (Art. 33(2) PCT).

2) Claims 1-4 lack novelty (Art. 33(2) PCT).
D1 (see p. 5, l. 28-40, ex. 3 and claims) discloses the cloning and the expression of the DNA coding for a *N. meningitidis* B protein from whole genomic DNA. D2 discloses various *N. Meningitidis* B ORFs (identified by means of nucleotide sequencing) and proteins encoded thereby (see p. 13, l. 2-p. 17, l. 3, ex. 1 and 2). Hence, both documents are based on a search for ORFs or protein-coding sequences within SEQ ID 1 and therefore anticipate the subject-matter of claim 1. The fact that the whole of the said sequence was not available does not mean that the search has not been carried out within the said sequence: it is assumed that the ORFs disclosed in the prior art as exemplified by D1 and D2 are to be found in the said sequence.
The same applies to claim 2, since identifying the initiation and termination codons is inherent in the definition of an ORF.
Claim 3 lacks novelty over D1 which discloses the cloning and expression of a *N. Meningitidis* protein.
The identification of a *N. Meningitidis* protein by means of an antibody recognising it is disclosed in D1, p. 44, l. 5-18, or D2, p. 33, l. 12-p. 40, l. 14: thus also claim 4 lacks novelty.

3) Claims 9-14,16-24 lack novelty (Art. 33(2) PCT).
SEQ ID 1 represents allegedly the full genomic sequence of *N. Meningitidis*. Both D1 and D2 disclose *N. meningitidis* proteins and nucleic acid fragments encoding them. They both use PCR to amplify a portion of the *Neisseria* genome.
Moreover, the fragments disclosed in D2 show no homology to any known gene (p. 51, l. 30-p. 52, l. 6) (as to claim 10, see also item VIII hereinbelow).

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/05928

Both D1 and D2, thus, anticipate the subject-matter of claims 9-15 and 18-23 in that they disclose fragments of the *N. Meningitidis* genome, probes, proteins, antibodies, compositions containing them and diagnostic uses thereof (see aforementioned passages).

Moreover, D1 discloses the therapeutic use of a *N. Meningitidis* protein and thus anticipates the subject-matter of claim 24.

- 4) Claims 16 and 17 lack novelty because a sequence contained in a computer, a computer memory or a computer storage medium is not a technical feature of the said products. Hence, any computer, computer memory or storage medium takes away the novelty of claims 16 and 17 (see also item VIII.2 hereinbelow).
- 5) Claims 7 and 8 lack an inventive step (Art. 33(3) PCT).
Independent of the assessment of the scientific merit of the sequencing work, and of the laboriousness and time required to achieve the result of sequencing the *N. Meningitidis* genome, no inventive merit can be acknowledged for the sequence SEQ ID 1 because it is the result of the direct application of standard, computerised techniques known in the art at the priority date of the application (see *Science*, v. 269, p. 496-512, 1995, p. 496, col. 3, l. 19-p. 508, col. 1, last full par.).
- 4) For the assessment of the present claims 22-24 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VII

Certain defects in the international application

- 1) Only published documents should be referred to in the application (Guidelines, II,

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/05928

4.17): citations such as those on p. 45, l. 6-7 or p. 46, l. 6-7 should thus be either deleted or amended.

Re item VIII

- 1) Claims 5, 6, 15 lack any technical feature and contravene thus the clarity requirement of Art. 6 PCT.
- 2) Claims 22-24 lack support (Art. 6 PCT) and their subject-matter contravenes Art. 5 PCT due to the absence of any example whatsoever as to a therapeutic application of the claimed sequence SEQ ID 1 or of any of the proteins or antibodies to which the claims relate.
- 3) Claim 10 lacks support (Art. 6 PCT) since no fragments of SEQ ID 1 or 1068 unique to *N. Meningitidis* are disclosed in the application. Moreover, the claim lacks clarity (Art. 6 PCT) because it merely relates to a *desideratum* without relating to any technical feature (e.g. a sequence) which would allow the obtention of the sought result.
- 4) Claim 20 lacks clarity (Art. 6 PCT) because SEQ ID 1 (which is longer than 2×10^6 bp (or a sequence having greater than 50% sequence identity therewith) cannot be used as a primer. Its reference to claims 7 and 8 should thus be deleted.

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

HARBIN, Alisa A. et al
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Intellectual Property - R440
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PCT

JUL 2001
Received
Chiron Corporation
Intellectual Property

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing
(day/month/year) 09.07.2001

Applicant's or agent's file reference
365.300

IMPORTANT NOTIFICATION

International application No.
PCT/US00/05928

International filing date (day/month/year)
08/03/2000

Priority date (day/month/year)
30/04/1999

Applicant
CHIRON CORPORATION et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

DOCKETED on/by 7/16/01 on
Att'y. AAH FA
File # P00365.300
Examiner
From: EPO

Name and mailing address of the IPEA/

European Patent Office
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Authorized officer

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 365.300	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/05928	International filing date (day/month/year) 08/03/2000	Priority date (day/month/year) 30/04/1999
International Patent Classification (IPC) or national classification and IPC C12Q1/68		
Applicant CHIRON CORPORATION et al.		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 8 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input checked="" type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application 		

Date of submission of the demand 22/11/2000	Date of completion of this report 09.07.2001
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Luzzatto, E Telephone No. +49 89 2399 8169



INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

International application No. PCT/US00/05928

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-69,71-122	as originally filed		
70	as received on	26/06/2000 with letter of	22/06/2000

Claims, No.:

1-24 as originally filed

Drawings, sheets:

1-18 as originally filed

Sequence listing part of the description, pages:

1-750, filed with the letter of 22.6.00

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

International application No. PCT/US00/05928

4. The amendments have resulted in the cancellation of:

the description, pages:
 the claims, Nos.:
 the drawings, sheets:

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

the entire international application.
 claims Nos. 5,6,15,24.

because:

the said international application, or the said claims Nos. 24 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for the said claims Nos. 5,6,15.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

the written form has not been furnished or does not comply with the standard.
 the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;

INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

International application No. PCT/US00/05928

citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 7,8
	No:	Claims 1-4,9-14,16-24
Inventive step (IS)	Yes:	Claims none
	No:	Claims 7,8
Industrial applicability (IA)	Yes:	Claims 1-23
	No:	Claims

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item I

Basis of the opinion

- 1) Sequence listing pages 1-750 filed with the letter of 22/6/00 do not form part of the application (Rule 13^{ter}.1(f) PCT).
- 2) Appendix A has been filed along with the application, however is not part of the description (Art. 3(2) PCT); it should therefore be changed into a figure or be deleted along with any reference thereto.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

- 1) Claims 5, 6 and 15 have not been searched and thus no opinion will be given with respect to whether their subject-matter meets the requirements of Art. 33 PCT. The same applies for claims 18-24 insofar as related to any of claims 5, 6, and 15.
- 2) Claims 1-4, 7-14, 18-24 have only been searched insofar as relating to SEQ ID 1 and will therefore be examined on the basis this limitation.
- 3) Claim 24 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).
- 4) Claims 16 and 17 have not been searched insofar as related to computer databases and will thus not be examined with respect to this feature.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1) D1 (EP-A-467714) and D2 (WO-A-9817805) disclose the purification of the entire genomic DNA of *N. Meningitidis* (see D1, ex. 3 and claims, D2, ex. 2, p. 54, l. 2-16, claims). They do not however disclose a sequence as that of SEQ ID 1, to which claims 7 and 8 relate. The subject-matter of the said claims is thus novel (Art. 33(2) PCT).
- 2) Claims 1-4 lack novelty (Art. 33(2) PCT).
D1 (see p. 5, l. 28-40, ex. 3 and claims) discloses the cloning and the expression of the DNA coding for a *N. meningitidis* B protein from whole genomic DNA. D2 discloses various *N. Meningitidis* B ORFs (identified by means of nucleotide sequencing) and proteins encoded thereby (see p. 13, l. 2-p. 17, l. 3, ex. 1 and 2). Hence, both documents are based on a search for ORFs or protein-coding sequences within SEQ ID 1 and therefore anticipate the subject-matter of claim 1. The fact that the whole of the said sequence was not available does not mean that the search has not been carried out within the said sequence: it is assumed that the ORFs disclosed in the prior art as exemplified by D1 and D2 are to be found in the said sequence.
The same applies to claim 2, since identifying the initiation and termination codons is inherent in the definition of an ORF.
Claim 3 lacks novelty over D1 which discloses the cloning and expression of a *N. Meningitidis* protein.
The identification of a *N. Meningitidis* protein by means of an antibody recognising it is disclosed in D1, p. 44, l. 5-18, or D2, p. 33, l. 12-p. 40, l. 14: thus also claim 4 lacks novelty.
- 3) Claims 9-14,16-24 lack novelty (Art. 33(2) PCT).
SEQ ID 1 represents allegedly the full genomic sequence of *N. Meningitidis*. Both D1 and D2 disclose *N. meningitidis* proteins and nucleic acid fragments encoding them. They both use PCR to amplify a portion of the *Neisseria* genome.
Moreover, the fragments disclosed in D2 show no homology to any known gene (p. 51, l. 30-p. 52, l. 6) (as to claim 10, see also item VIII hereinbelow).

Both D1 and D2, thus, anticipate the subject-matter of claims 9-15 and 18-23 in that they disclose fragments of the *N. Meningitidis* genome, probes, proteins, antibodies, compositions containing them and diagnostic uses thereof (see aforementioned passages).

Moreover, D1 discloses the therapeutic use of a *N. Meningitidis* protein and thus anticipates the subject-matter of claim 24.

- 4) Claims 16 and 17 lack novelty because a sequence contained in a computer, a computer memory or a computer storage medium is not a technical feature of the said products. Hence, any computer, computer memory or storage medium takes away the novelty of claims 16 and 17 (see also item VIII.2 hereinbelow).
- 5) Claims 7 and 8 lack an inventive step (Art. 33(3) PCT).
Independent of the assessment of the scientific merit of the sequencing work, and of the laboriousness and time required to achieve the result of sequencing the *N. Meningitidis* genome, no inventive merit can be acknowledged for the sequence SEQ ID 1 because it is the result of the direct application of standard, computerised techniques known in the art at the priority date of the application (see *Science*, v. 269, p. 496-512, 1995, p. 496, col. 3, l. 19-p. 508, col. 1, last full par.).
- 4) For the assessment of the present claims 22-24 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VII

Certain defects in the international application

- 1) Only published documents should be referred to in the application (Guidelines, II,

4.17): citations such as those on p. 45, l. 6-7 or p. 46, l. 6-7 should thus be either deleted or amended.

Re item VIII

- 1) Claims 5, 6, 15 lack any technical feature and contravene thus the clarity requirement of Art. 6 PCT.
- 2) Claims 22-24 lack support (Art. 6 PCT) and their subject-matter contravenes Art. 5 PCT due to the absence of any example whatsoever as to a therapeutic application of the claimed sequence SEQ ID 1 or of any of the proteins or antibodies to which the claims relate.
- 3) Claim 10 lacks support (Art. 6 PCT) since no fragments of SEQ ID 1 or 1068 unique to *N. Meningitidis* are disclosed in the application. Moreover, the claim lacks clarity (Art. 6 PCT) because it merely relates to a *desideratum* without relating to any technical feature (e.g. a sequence) which would allow the obtention of the sought result.
- 4) Claim 20 lacks clarity (Art. 6 PCT) because SEQ ID 1 (which is longer than 2×10^6 bp (or a sequence having greater than 50% sequence identity therewith) cannot be used as a primer. Its reference to claims 7 and 8 should thus be deleted.